PATENT COOPERATION TREA

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-32730A/30731	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/11555	International filing date *(day/month/year)* 17.10.2003	Priority date *(day/month/year)* 17.10.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/196		
Applicant NOVARTIS AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04.05.2004	10.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Collura, A Telephone No. +49 89 2399-7870

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/11555

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-31 as originally filed

Claims, Numbers

1-16 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 4,6-8,12,14-16 (with respect to IA)

   because:

   ☒ the said international application, or the said claims Nos. 4,6-8,12,14-16 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-3,5,9-11,13
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 4, 6-8, 12 and 14-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: 'Strategies to control pain in older persons: Highlights of recent guidelines' CONSULTANT 15 SEP 2002 UNITED STATES, vol. 42, no. 11, 15 September 2002 (2002-09-15), pages 1373-1376, XP009025747 ISSN: 0010-7069

D2: FREEDMAN G M: 'CLINICAL MANAGEMENT OF COMMON CAUSES OF GERIATRIC PAIN' GERIATRICS, ADVANSTAR COMMUNICATIONS, CLEVELAND, OH, US, vol. 57, no. 5, May 2002 (2002-05), pages 36-42, XP009010328 ISSN: 0016-867X

D3: HARDEN R N: 'Complex regional pain syndrome' BRITISH JOURNAL OF ANAESTHESIA, vol. 87, no. 1, July 2001 (2001-07), pages 99-106, XP002269885 ISSN: 0007-0912

D4: SIMANSKI C ET AL: '[Acute pain therapy and management in orthopedics]' DER ORTHOPADE. GERMANY MAY 2002, vol. 31, no. 5, May 2002 (2002-05), pages 522-532;quiz 532 - 533, XP002269886 ISSN: 0085-4530

D5: GLOTH F MICHAEL III: 'Pain management in older adults: Prevention and treatment' JOURNAL OF THE AMERICAN GERIATRICS SOCIETY, vol. 49, no. 2, February 2001 (2001-02), pages 188-199, XP002232826 ISSN: 0002-8614

For what concerns the most relevant paragraphs of the above-mentioned documents,

please see citations in the International Search Report, unless otherwise indicated.

1. NOVELTY

Claims 1-16 appear to fulfill the requirements of Art. 33(1) and (2) PCT because they seem not to be anticipated by the available prior art documents.

2. INVENTIVE STEP

Claims 1-16 don't appear to fulfill the requirements of Art. 33(1) and (3) PCT because they don't appear to be inventive.

Document **D1** discloses (cf. Page 1367) that Cox-2 inhibitors (i.e. rofecoxib and celecoxib) are used for the treatment of pain in older persons and that anticonvulsants (i.e. carbamazepine) can be used in combination with said analgesics especially for managing neuropathic pain. D1 also states that newer anticonvulsants have a low incidence of adverse effects and they should be preferred to tricyclic antidepressants.

The same disclosure is given by **D2** which also states that "by combining medications, individual doses can be decreased, thereby minimizing the risk of side effects" and that "choosing agents that work on the pain pathways at different points will yield to additive or synergistic effect".

Document **D3**, on the same line of D1 and D2, describes the use of "rational polypharmacy" for the treatment of CRPS, that means the combination of drugs that make sense together (i.e. anti-inflammatory and centrally acting GABAergic agents among which carbamazepine and oxcarbazepine are mentioned).

D4 describes pain therapy in orthopaedics and, in particular, the use of Cox-2 inhibitors (i.e. celecoxib and rofecoxib) together with co-analgesics (i.e. carbamazepine).

D5 as well describes a combination therapy for treating pain.

It has to be noted by the Applicant that no identification of the technical problem is provided in the description and therefore the application does not fulfil the requirements of Rule 5.1(iii) PCT.

According to what is already part of the state of the art, the IPEA considers the

technical problem as being the provision of a combination therapy of anti-pain actives, which acts according to different biochemical paths, so to minimize the risk of side effects.
The solution proposed in the present application, namely the provision of a pharmaceutical composition comprising an anticonvulsant and a Cox-2 inhibitors, cannot be considered as involving an inventive step since it has been already suggested by D1-D5.
The person skilled in the art would have chosen one representative of the Cox-2 inhibitor class and one of the anticonvulsant class for obtaining the claimed composition without the exercise of any inventive ability.
Moreover, no surprising effect is shown by choosing two particular actives (namely, lumiracoxib or Prexige® and oxacarbazepine or Trileptal®) compared to others.

3. INDUSTRIAL APPLICABILITY

For the assessment of the present claims 4, 6-8, 12 and 14-16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. FURTHER ITEMS

4.1 It has to be noted by the Applicant that, in the present description, there is no mention of the prior art nor of any problem to be solved.
4.2 The "incorporation by reference" of documents or parts of documents is not allowed because it doesn't clearly define the scope for which protection is sought. The description should therefore be amended in order to overcome this objection.
4.3 The subject-matter of claims 2 and 3 and claims 10 and 11 appears to be redundant.